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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,783	12/24/2001	Michael Graupc	1016US	3968

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EXAMINER

SHIAO, REI TSANG

ART UNIT

PAPER NUMBER

1626

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/035,783	Applicant(s) GRAUPE ET AL.	
	Examiner Robert Shiao	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on responses filed on 9/25, 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 and 31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-29 and 31 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This application claims benefit of the provisional application: 60, 257,603 with a filing date 12/22/2000.
2. Cancellation of claim 30 in Paper No. 9003, dated September 15, 2003, is acknowledged. Claims 1-29, and 31 are pending in the application.
3. The previous restriction requirement of Paper No. 1102, dated November 6, 2002, has been modified as follows.

Election/Restriction

4. The Markush group set forth in the claims includes both independent and distinct inventions, and patentably distinct compounds (or species) within each invention. However, this application discloses and claims a plurality of patentably distinct inventions far too numerous to list individually. Moreover, each of these inventions contains a plurality of patentably distinct compounds, also far too numerous to list individually. For these reasons provided below, restriction to one of the following Groups is required under 35 U.S.C. 121, wherein an Group is a set of patentably distinct inventions of a broad statutory category (e.g. Compounds, Methods of Use, Methods of Making, etc.):

- I. Claims 1-28, in part, drawn to compounds/compositions of formula (I) having variables X_1 , R^3 , and R^4 , X_1 represents $-C(R^1)(R^2)X^2$, wherein X^2 is as defined in claim 1, wherein hetero(C₄-C₁₀)aryl or hetero(C₄-C₁₀)cycloalkyl of X^2 represents

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represents pyran, thiopyran, pyrimidine, thiazole, isothiazole, pyridine, furan, imidazole, isoxazole, oxadiazole, oxazole, or triazole thereof;

R¹ and R² are as defined in claim 1, except: R¹ and R² independently do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene or R¹ and R² independently is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene, R¹ and R² taken together with the carbon atom do not form hetero(C₃-C₈)cycloalkylene;

R³ represents -C(R¹⁶)(R¹⁷)X⁷, R¹⁶ and R¹⁷ independently represent hydrogen, alkyl, fluoro, or hydroxy; X⁷ is as defined in claim 1 except: X⁷ do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene, and X⁷ is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; and

R⁴ represents -C(R¹⁶)(R¹⁷)X⁷, R¹⁶ and R¹⁷ independently represent hydrogen, alkyl, fluoro, or hydroxy; X⁷ represents -R¹⁵, -X⁴OR¹⁵, -X⁴SR¹⁵, -X⁴S(O)R¹⁵, -X⁴S(O)₂R¹⁵, -X⁴C(O)R¹⁵, -X⁴C(O)OR¹⁵, -X⁴OC(O)R¹⁵, -X⁴NR¹⁵R¹², -X⁴NR¹²C(O)R¹⁵, -X⁴NR¹²C(O)OR¹⁵, -X⁴NC(O)NR¹⁵R¹², -X⁴NR¹²S(O)₂R¹⁵, -X⁴NR¹²C(O)NR¹⁵R¹², or -X⁴NR¹²C(NR¹²)NR¹⁵R¹², and X⁴ represents a bond or alkylene, R¹² represents hydrogen or alkyl, R¹⁵ is as defined in claim 1 except: wherein R¹⁵ does not represent hetero(C₅-C₁₀)aryl(C₀-C₆)alkyl or hetero(C₈-C₁₂)bicycloaryl(C₀-C₆)alkyl, and wherein the hetero(C₃-C₁₀)cycloalkyl of R¹⁵ represents **morpholinyl** thereof, and X⁷ is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; classified in classes 514/544, numerous subclasses.

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- II. Claims 1-28, in part, drawn to compounds/compositions of formula (I) having variables X_1 , R^3 , and R^4 , X_1 represents $-C(R^1)(R^2)X^2$, wherein X^2 is as defined in claim 1, except: X^2 does not represent hetero(C_4 - C_{10})aryl(C_0 - C_6)alkyl or hetero(C_4 - C_{10})cycloalkyl or substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene, R^9 of X^2 does not represent hetero(C_5 - C_{10})aryl(C_0 - C_6)alkyl; R^1 and R^2 are as defined in claim 1, except: R^1 and R^2 independently do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene or R^1 and R^2 independently is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene, and R^1 and R^2 taken together with the carbon atom form hetero(C_3 - C_8)cycloalkylene **azepane**;
- R^3 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 is as defined in claim 1 except: X^7 do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; and
- R^4 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 represents $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4NC(O)NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$, or $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, and X^4 represents a bond or alkylene, R^{12} represents hydrogen or alkyl, R^{15} is as defined in claim 1 except: wherein R^{15} does not represent hetero(C_5 - C_{10})aryl(C_0 - C_6)alkyl or hetero(C_8 - C_{12})bicycloaryl(C_0 - C_6)alkyl, and wherein the hetero(C_3 - C_{10})cycloalkyl of R^{15}

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represents **morpholinyl** thereof, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; classified in classes 514/540, numerous subclasses.

III. Claims 1-28, in part, drawn to compounds/compositions of formula (I) having variables X_1 , R^3 , and R^4 , X_1 represents $-C(R^1)(R^2)X^2$, wherein X^2 is as defined in claim 1, except: wherein hetero(C_4 - C_{10})aryl or hetero(C_4 - C_{10})cycloalkyl of X^2 represents thiazole, isothiazole, imidazole, isoxazole, oxadiazole, oxazole, or triazole thereof;

R^1 and R^2 are as defined in claim 1, except: R^1 and R^2 independently do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene or R^1 and R^2 independently is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene, and R^1 and R^2 taken together with the carbon atom do not form hetero(C_3 - C_8)cycloalkylene;

R^3 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 is as defined in claim 1 except: X^7 do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; and

R^4 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 represents $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4NC(O)NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$,

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$-X^4NR^{12}C(O)NR^{15}R^{12}$, or $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, and X^4 represents a bond or alkylene, R^{12} represents hydrogen or alkyl, R^{15} is as defined in claim 1 except: wherein R^{15} does not represent hetero(C_5-C_{10})aryl(C_0-C_6)alkyl or hetero(C_8-C_{12})bicycloaryl(C_0-C_6)alkyl, and wherein the hetero(C_3-C_{10})cycloalkyl of R^{15} represents **pyrrolidine**, **pyran**, **thiopyran** thereof, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; classified in classes 514/548, numerous subclasses.

- IV. Claims 1-28, in part, drawn to compounds/compositions of formula (I) having variables X_1 , R^3 , and R^4 , X_1 represents $-C(R^1)(R^2)X^2$, wherein X^2 is as defined in claim 1, except: wherein hetero(C_4-C_{10})aryl or hetero(C_4-C_{10})cycloalkyl of X^2 represents thiazole, isothiazole, imidazole, isoxazole, oxadiazole, oxazole, or triazole thereof;
- R^1 and R^2 are as defined in claim 1, except: R^1 and R^2 independently do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene or R^1 and R^2 independently is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene, or R^1 and R^2 taken together with the carbon atom form a moiety having heteroaryl **pyridine** thereof;
- R^3 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 is as defined in claim 1 except: X^7 do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; and

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R^4 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 represents $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4NC(O)NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$, or $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, and X^4 represents a bond or alkylene, R^{12} represents hydrogen or alkyl, R^{15} is as defined in claim 1 except: wherein R^{15} does not represent hetero(C_5 - C_{10})aryl(C_0 - C_6)alkyl or hetero(C_8 - C_{12})bicycloaryl(C_0 - C_6)alkyl, and wherein the hetero(C_3 - C_{10})cycloalkyl of R^{15} represents **piperidine** thereof, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; classified in classes 514/546, numerous subclasses.

- V. Claims 1-28, in part, drawn to compounds/compositions of formula (I) having variables X_1 , R^3 , and R^4 , X_1 represents $-C(R^1)(R^2)X^2$, wherein X^2 is as defined in claim 1, except: wherein hetero(C_4 - C_{10})aryl or hetero(C_4 - C_{10})cycloalkyl of X^2 represents thiazole, isothiazole, imidazole, isoxazole, oxadiazole, oxazole, or triazole thereof;
- R^1 and R^2 are as defined in claim 1, except: R^1 and R^2 independently do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene or R^1 and R^2 independently is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene, R^1 and R^2 taken together with the carbon atom do not form hetero(C_3 - C_8)cycloalkylene;

R^3 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 is as defined in claim 1 except: wherein hetero(C_5-C_{10})aryl, hetero(C_8-C_{12})bicycloaryl, or hetero(C_3-C_{10})cycloalkyl of X^7 represents **pyrrolidine, pyran, thiopyran** thereof, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene;

R^4 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 is as defined in claim 1 except: X^7 do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; classified in classes 514/548, numerous subclasses.

VI. Claims 1-28, in part, drawn to compounds/compositions of formula (I) having variables X_1 , R^3 , and R^4 , X_1 represents $-C(R^1)(R^2)X^2$, wherein X^2 is as defined in claim 1, except: wherein hetero(C_4-C_{10})aryl or hetero(C_4-C_{10})cycloalkyl of X^2 represents thiazole, isothiazole, imidazole, isoxazole, oxadiazole, oxazole, or triazole thereof;

R^1 and R^2 are as defined in claim 1, except: R^1 and R^2 independently do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene or R^1 and R^2 independently is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene, R^1 and R^2 taken together with the carbon atom do not form hetero(C_3-C_8)cycloalkylene;

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R^3 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 represents $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4NC(O)NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$, or $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, and X^4 represents a bond or alkylene, R^{12} represents hydrogen or alkyl, R^{15} is as defined in claim 1 except: wherein R^{15} does not represent hetero(C_5-C_{10})aryl(C_0-C_6)alkyl or hetero(C_8-C_{12})bicycloaryl(C_0-C_6)alkyl, and wherein the hetero(C_3-C_{10})cycloalkyl of R^{15} represents **piperidine** thereof, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; and

R^4 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 is as defined in claim 1 except: X^7 do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; classified in classes 514/546, numerous subclasses.

- VII. Claims 1-28, in part, drawn to compounds/compositions of formula (I) having variables X_1 , R^3 , and R^4 , X_1 represents $-C(R^1)(R^2)X^2$, wherein X^2 is as defined in claim 1, except: wherein hetero(C_4-C_{10})aryl or hetero(C_4-C_{10})cycloalkyl of X^2 represents thiazole, isothiazole, imidazole, isoxazole, oxadiazole, oxazole, or triazole thereof;

R¹ and R² are as defined in claim 1, except: R¹ and R² independently do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene or R¹ and R² independently is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene, or R¹ and R² taken together with the carbon atom form a moiety having heterocycloalkylene **pyran or piperidine** thereof;

R³ represents -C(R¹⁶)(R¹⁷)X⁷, R¹⁶ and R¹⁷ independently represent hydrogen, alkyl, fluoro, or hydroxy; X⁷ is as defined in claim 1 except: X⁷ do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene, and X⁷ is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; and

R⁴ represents -C(R¹⁶)(R¹⁷)X⁷, R¹⁶ and R¹⁷ independently represent hydrogen, alkyl, fluoro, or hydroxy; X⁷ is as defined in claim 1 except: X⁷ do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene, or X⁷ is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; classified in classes 514/546/548, numerous subclasses.

- VIII. Claims 1-28, in part, drawn to compounds/compositions of formula (I) having variables X₁, R³, and R⁴, X₁ represents X³, wherein X³ represents the formula (a), wherein the variable n is 1; Z is 0 or 1; X⁵ represents NR¹⁰, S or O, and R¹⁰ is as defined in claim 1, except: R¹⁰ does not represent hetero(C₃-C₁₀)cycloalkyl(C₀-C₃)alkyl, hetero(C₅-C₁₀)aryl(C₀-C₆)alkyl, or hetero(C₅-C₁₀)bicycloaryl(C₀-C₆)alkyl and R¹⁰ is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; X⁶ represents NR¹¹, S or O, and R¹¹ is

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as defined in claim 1, except: R^{11} does not represent hetero(C_3 - C_{10})cycloalkyl(C_0 - C_3)alkyl, hetero(C_5 - C_{10})aryl(C_0 - C_6)alkyl, or hetero(C_5 - C_{10})bicycloaryl(C_0 - C_6)alkyl and R^{11} is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene;

R^3 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 is as defined in claim 1 except: X^7 do not represent heteroaryl, heterocycloalkyl, or heterocycloalkylene, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; and

R^4 represents $-C(R^{16})(R^{17})X^7$, R^{16} and R^{17} independently represent hydrogen, alkyl, fluoro, or hydroxy; X^7 represents $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4NC(O)NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$, or $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, and X^4 represents a bond or alkylene, R^{12} represents hydrogen or alkyl, R^{15} is as defined in claim 1 except: wherein R^{15} does not represent hetero(C_5 - C_{10})aryl(C_0 - C_6)alkyl or hetero(C_8 - C_{12})bicycloaryl(C_0 - C_6)alkyl, and wherein the hetero(C_3 - C_{10})cycloalkyl of R^{15} represents **morpholinyl** thereof, and X^7 is not substituted with heteroaryl, heterocycloalkyl, or heterocycloalkylene; classified in classes 514/544, numerous subclasses.

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- IX. Claims 1-28, in part, drawn to compounds/compositions of formula (I), is receiving compounds not encompassed by Groups I-VIII, classified in class 558/564/585/514, numerous subclasses.
- X. Claim 29, drawn to methods of use of formula (I) (treating arthritis, muscular dystrophy, glomerulonephritis, etc), classified in class 514, numerous subclasses.
- XI. Claim 31, drawn to a process of making a compound of formula (I), classified in class 544/546/548, numerous subclasses.

In addition to an election of one of Invention Sets I-II above, restriction is further required under 35 U.S.C. 121 as follows:

If Group X is elected, then election of one of the following methods of use is required:

- A. Method of treating arthritis
- B. Method of treating muscular dystrophy
- C. Method of treating glomerulonephritis

In accordance with the decisions in *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984),

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restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other member(s) obvious under 35 U.S.C. 103.

Where an election of any one of Groups I-XI is made, an election of a single compound (or set of compounds) is further required including an exact definition of each substitution on the base molecule (Formula I), wherein a single member at each substituent group or moiety is selected. For example, if a base molecule has a substituent group X_1 , wherein X_1 is recited to be any one of $-C(R^1)(R^2)X^2$ or X^3 , and R^1 or R^2 represents hydrogen or fluoro, X^2 represent cyano, $-CHO$, etc., then applicant must select a single substituent for $-C(R^1)(R^2)X^2$ or X^3 , for example, R^1 and R^2 represent hydrogen, and X^2 represents CHO , and each subsequent variable position. In the instant case, upon election of a single compound (or set of compounds), the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected compound (compounds which are so similar thereto as to be within the same inventive concept and reduction to practice). The scope of an independent invention will encompass all compounds within the scope of the claim which fall into the same class and subclass as the elected compound (or set

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of compounds), but may also include additional compounds which fall in related subclasses. Examination will then proceed on the elected compound AND the entire scope of the invention encompassing the elected compound as defined by common classification. A clear statement of the examined invention, defined by those class(es) and subclass(es) will be set forth in the first action on the merits. Note that the restriction requirement will not be made final until such time as applicant is informed of the full scope of compounds along with process of using said compound under examination. This will be set forth by reference to specific class(es) and subclass(es) examined. Should applicant traverse on the ground that the compounds are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the compounds to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C 103(a) of the other.

All compounds falling outside the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to nonelected subject matter and will be withdrawn from consideration under 35 U.S.C. 121 and 37 C.F.R. 1.142(b). Applicant may reserve the right to file divisional applications on the remaining subject matter. The provisions of 35 U.S.C. 121 apply with regard to double patenting covering divisional applications.

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventors must be amended in compliance with 37C.F.R. 1.48(b) if one of the

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currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R. 1.48(b) and by the fee required under 37CFR 1.17(i).

If desired upon election of a single compound, applicants can review the claims and disclosure to determine the scope of the invention and can **set forth** a group of compounds which are so similar within the same inventive concept and reduction to practice. Markush claims must be provided with support in the disclosure for each member of the Markush group. See MPEP 608.01(p). Applicant should exercise caution in making a selection of a single member for each substituent group on the base molecule to be consistent with the written description.

Rationale Establishing Patentable Distinctiveness Within Each Group

Each Invention Set listed above is directed to or involves the use or making of compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP 806.04, MPEP 808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over either of the other inventions, i.e. they are patentable over each other. Chemical structures which are similar are presumed to function similarly, whereas chemical structures that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrebuttable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance

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with the holdings of Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Lulu, 223 USPQ 1257 (Fed. Cir. 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

The above Groups represent general areas wherein the inventions are independent and distinct, each from the other because of the following reasons:

Each of Groups I-IX are distinct and independent, one from the other on the basis of structure defined in the claimed compounds as directed to a compound of formula I having various heterocyclyl or heteroaryl moieties. Absent factual evidence to the contrary, each is a different chemical compound.

Groups I-IX and X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using the product (MPEP 806.05(h)). In the instant case, the simple compound 1,2,3-propanetricarboxamide, N,N',N''-tris(2-hydroxypropyl)-, as claimed can be used in a materially different process of using, i.e., skin moisturizers, see RN: 64165-49-7 of CAS:87:157007. The instant morpholine compounds are as demonstrated throughout the specification and in claims 1-28 which are directed to several different methods of using the morpholine compounds, for example treating arthritis.

Groups I-IX and XI are independent and distinct products and processes of making because, compounds of Group I-IX and processes of making of Group XI differ in elements, bonding arrangement and chemical property (i.e., starting materials, reacting conditions) to such an extent that a reference anticipating compounds of any one group would not render another group obvious.

Groups X and XI are independent and distinct processes of making and methods of use because, processes of making of Group XI and methods of use Group X differ in elements, bonding arrangement and chemical property (i.e., starting materials), administration (i.e., dose) to such an extent that a reference anticipating compounds of any one group would not render another group obvious.

In addition, because of the plethora of classes and subclasses in each of the Groups, a serious burden is imposed on the examiner to perform a complete search of the defined areas. Therefore, because of the reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden in the examination of this application.

Advisory of Rejoinder

5. The following is a recitation of M.P.E.P. §821.04, Rejoinder:

Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 809.02 (c) and § 821 through § 821.03. However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

Where product and process claims are presented in a single application and that application qualifies under the transitional restriction practice pursuant to

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37 CFR 1.129(b), applicant may either (1) elect the invention to be searched and examined and pay the fee set forth in 37 CFR 1.17(s) and have the additional inventions searched and examined under 37 CFR 1.129(b)(2), or (2) elect the invention to be searched and examined and not pay the additional fee (37 CFR 1.129(b)(3)).

Where no additional fee is paid, if the elected invention is directed to the product and the claims directed to the product are subsequently found patentable, process claims which either depend from or include all the limitations of the allowable product will be rejoined. If applicant chooses to pay the fees to have the additional inventions searched and examined pursuant to 37 CFR 1.129(b)(2), even if the product is found allowable, applicant would not be entitled to a refund of the fees paid under 37 CFR 1.129(b) by arguing that the process claims could have been rejoined. 37 CFR 1.26 states that "money paid by actual mistake or in excess will be refunded, but a mere change of purpose after the payment of money...will not entitle a party to demand such a return..." The fees paid under 37 CFR 1.129(b) were not paid by actual mistake nor paid in excess, therefore, applicant would not be entitled to a refund.

In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104 - 1.106. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

The following is a recitation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. §103(b)" (1184 TMOG 86(March 26, 1996)):

"However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim **depends from or otherwise includes all the limitations of** an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined." (emphasis added)

Therefore, in accordance with M.P.E.P. §821.04 and *In re Ochiai*, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Shiao whose telephone number is (703) 308-4002. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (703) 308-4537. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

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305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196

A handwritten signature in cursive script, appearing to read "R. Desai", followed by a horizontal line and two dots.A handwritten word "for" in cursive script, positioned to the left of the typed name.

Joseph K. McKane
Supervisory Patent Examiner
Art Unit 1626

Handwritten initials "R.S." in cursive script.

Robert Shiao, Ph.D.
Patent Examiner
Art Unit 1626

December 15, 2003